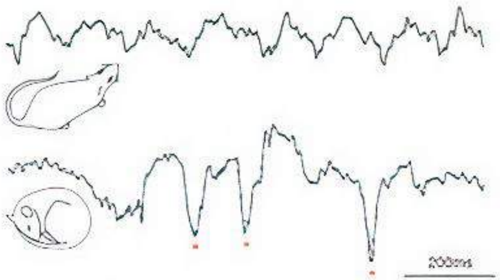
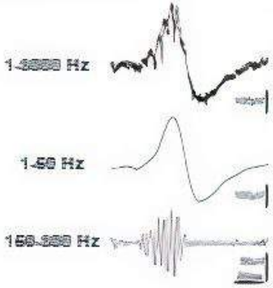
Abstract

Sharp wave-ripple complexes (SWRs) are hippocampal network phenomena involved in memory consolidation. To date, the mechanisms underlying their occurrence remain obscure.



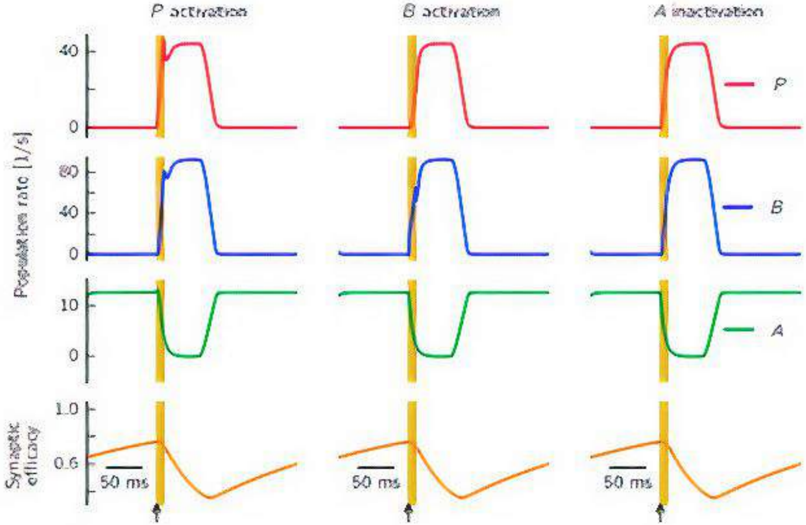
adapted from
Girardeau and Zugaro (2011)



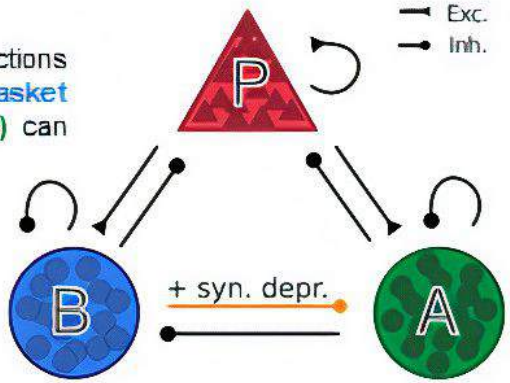
adapted from
Maier et al. (2003)

Our model predicts transient SWRs can be generated when activating *P* (left) and *B* (middle) cells, as experimentally reported.

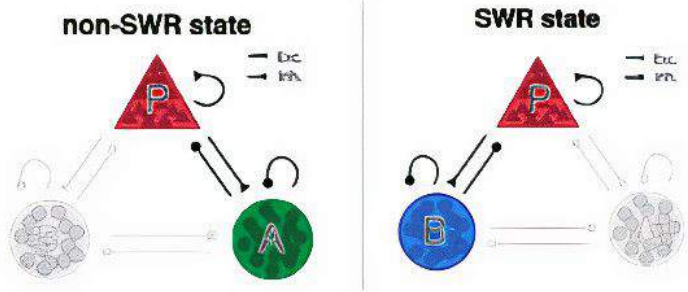
Furthermore, we predict that the silencing of *A* cells can trigger SWRs (right).



In Evangelista et al. (2020)[1], we show how the interactions between pyramidal cells (*P*), parvalbumin-positive (PV⁺) basket cells (*B*), and an unidentified class of anti-SWR cells (*A*) can contribute to the initiation and termination of SWRs.



In our network of spiking neurons and its rate-model approximation, sharp-waves emerge from the competition between the two interneuron populations and the resulting disinhibition of pyramidal cells, regulated by a short-term synaptic depression in the $B \rightarrow A$ connection.



Related publication:

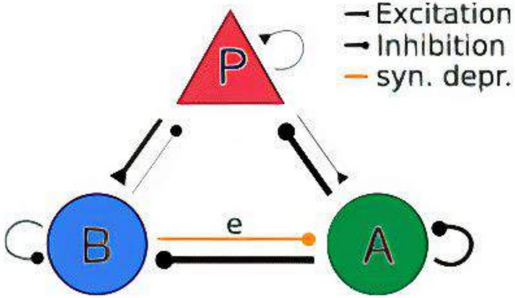
[1] R. Evangelista *et al*, JNeurosci 40(41):7811–7836, 2020

Techniques & Methods

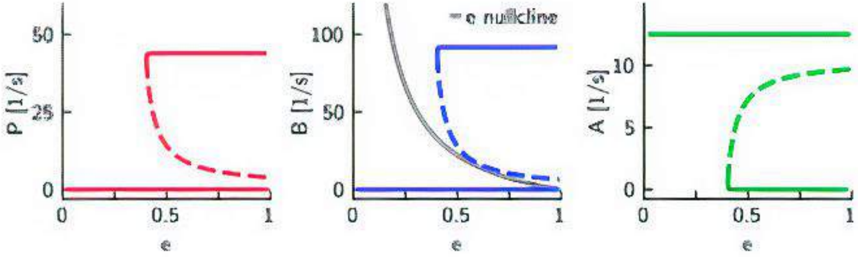
Rate model equations

$$\tau_P \frac{\partial P}{\partial t} = -P + f_P(W_{PP}P - W_{PB}B - W_{PA}A)$$
$$\tau_B \frac{\partial B}{\partial t} = -B + f_B(W_{BP}P - W_{BB}B - W_{BA}A)$$
$$\tau_A \frac{\partial A}{\partial t} = -A + f_A(W_{AP}P - W_{AB}Be - W_{AA}A)$$

$f_I(x)$, $I \in \{P, B, A\}$ are the soft-plus activation functions



Line width is proportional to the 'default' value of the connection strengths W_{IJ}, derived from the spiking network as the best approximation to experiments.



Steady-state rates of P, B, and A as a function of synaptic efficacy e in the $B \rightarrow A$ connection. Solid and dashed colored curves depict stable and unstable fixed points, respectively.

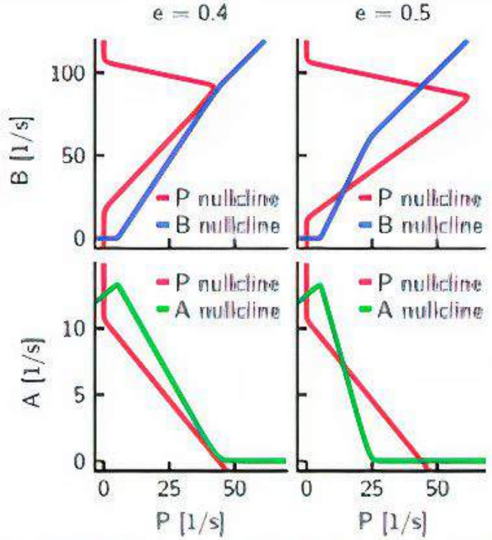
$e > 0.4$, bistability: SWR and non-SWR states coexist, separated by an unstable threshold.

$e < 0.4$, monostability: only non-SWR state exists.

Short-term depression: $$\frac{\partial e}{\partial t} = \frac{1-e}{\tau_d} - \eta B e$$

Adding a short-term depression mechanism in the $B \rightarrow A$ connection allows for the existence of transient SWR events:

- In the non-SWR state ($B = 0$), e will increase, bringing the system closer to the threshold and making it excitable upon current stimulation;
- In the SWR state ($B > 0$), e will decrease, terminating the SWR event when reaching the bifurcation point.



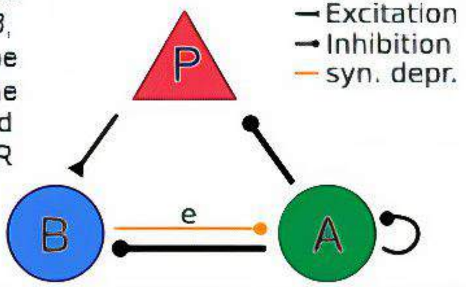
Nullclines (with third population in steady state) show transition from 1 to 3 steady states.

Results 1

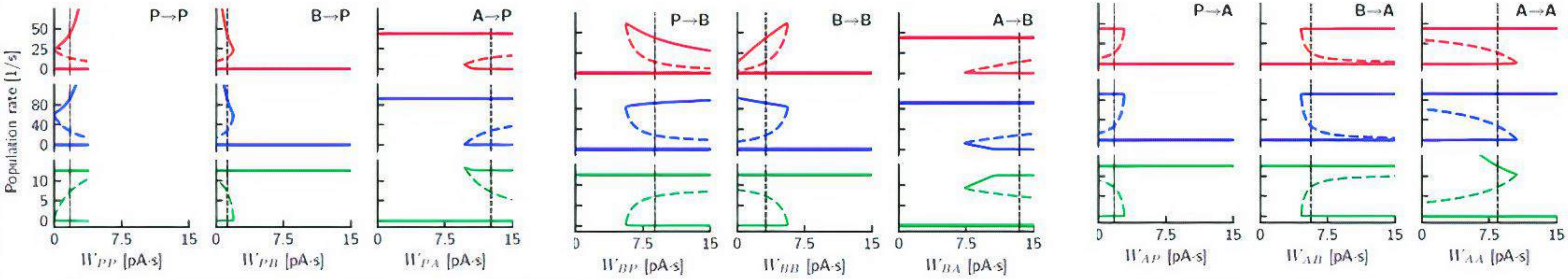
Bifurcation analysis with respect to each W_{IJ} connection strength shows the role each of them plays in the model dynamics:

- $P \to P$, $B \to B$, $P \to B$, and $B \to P$ regulate the population rates of P and B in the SWR state;
- $A \to P$ and $A \to B$ do not affect population rates, but must be large enough to ensure bistability;
- $A \to A$ must be small enough to ensure bistability, but large enough for the non-SWR state to remain close to the threshold, i.e., excitable.

A minimal network with only the 5 connections $A \to P$, $A \to B$, $P \to B$, $B \to A$, $A \to A$ would be sufficient to preserve the model's excitability and generate transient SWR events if stimulated.

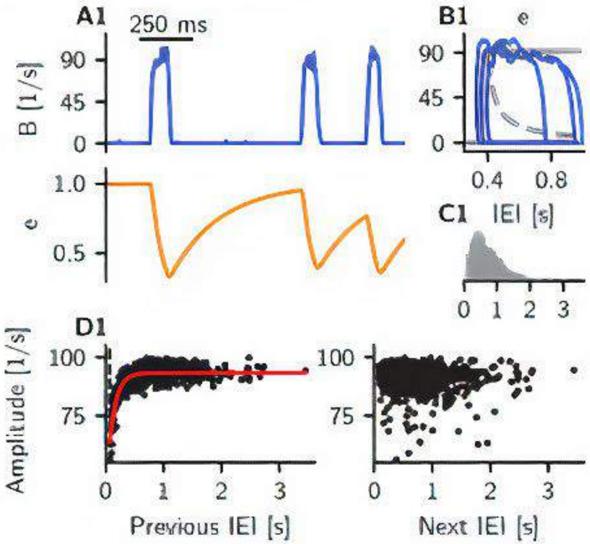


The vertical dashed lines are the 'default' values.



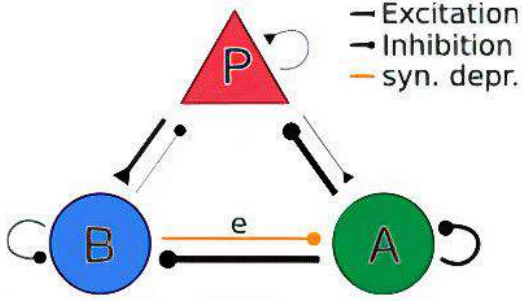
Results 2

By itself, the rate model cannot generate 'Spontaneous' events. For this, we add noise to the current input of the three populations, mimicking synaptic current updates in the non-SWR state.



In agreement with experimental results, we observe: (1) a strong correlation between the event Amplitude and the Previous Inter-Event-Interval (IEI) and (2) no correlation between Amplitude and Next IEI.

Conclusions



Our models explain how the activation of pyramidal cells or PV⁺ basket cells can trigger SWRs, as shown *in vitro*, and suggest that PV⁺ cell-mediated short-term synaptic depression influences the experimentally reported dynamics of SWR events. Furthermore, we predict that the silencing of anti-SWR interneurons can trigger SWRs.

Bifurcation analysis of the rate model shows the existence of a bistable configuration as a general property of such networks, robust to changes in model parameters, and useful to better understand the principles governing SWR generation in this type of disinhibitory network.